REMARKS

Applicants thank the Examiner for the very thorough consideration given the present application. Claims 1-3 are now present in this application. No new matter has been added by way of the present amendment. For instance, claim 1 has been amended to more clearly point out the subject matter claimed, as requested by the Examiner. Support for this amendment can be found at page 6, lines 14-22 and page 8, lines 9-28. Accordingly, no new matter has been added.

At the outset, the present application is believed to be in condition for allowance. Entry of the accompanying amendment is requested under 37 C.F.R. §1.116, as the amendment does not raise any new issues which would require further search and/or consideration by the Examiner. Furthermore, Applicants request entry of this amendment in order to place the claims in better form for consideration on Appeal.

In view of the following amendments and remarks, Applicants respectfully request that the Examiner withdraw all outstanding rejections and allow the currently pending claims.

Issues Under 35 U.S.C.§112, 2nd paragraph

Claims 1-3 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner asserts that the phrase "supporting substances" is unclear.

Claim 1 has been amended to eliminate the phrase "supporting substances". Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. § 102(e)

Claim 1 stands rejected under 35 U.S.C. § 102(e) as being anticipated by Darko (U.S. 6,342,530) (hereinafter Darko '530). This rejection is respectfully traversed.

The Examiner asserts that Darko '530 discloses a pharmaceutical composition suitable for parenteral administration having anti-inflammatory and analgesic property, characterized in that it contains an alkylammonium salt of a 2-arylpropionic acid in an aqueous solution, said solution being free of preservatives, co-solvents and supporting substances. The Examiner asserts that Table 1 in Darko '530 discloses that the solution has a pH in the range of from 8 to 9. Applicants respectfully disagree.

Darko '530 is directed to a pharmaceutical composition consisting of a therapeutically effective amount of d,l or l-lysine salt of R,S or S-ibuprofen dissolved in sterile water. Darko '530 does not disclose that the solution is maintained at a pH of from 8 to 9, or that the solution is formulated for parenteral use or results in pain-free administration.

Consideration of the reference as a whole shows that Table 1 merely provides data recorded as the solution for injection was being prepared. See, for example, col. 4, line 66 to col. 5, line 2. This portion of the text makes clear that the solution is mixed, the pH is measured and the pH is again adjusted. One skilled in the art would not be motivated to **maintain** (emphasis added) a pH of from 8 to 9 in view of the disclosure of Darko '530 for lack of written description of this feature. Furthermore, Applicants respectfully submit that Table 1 in Darko '530 merely discloses the pH of "pooled samples" and not the final **parenteral compositions** (emphasis added) that, at some **unknown** (emphasis added) point in time, had a pH of 6.5 to 8.5. These samples do not necessarily correspond to actual parenteral compositions administered to patients.

In contrast, Example 4 of Darko '530, when describing a method for preparing a parenteral composition, explicitly discloses that the pH is adjusted to 7.2 to 7.6 and again re-adjusted to the same level. Clearly, a pH of 7.2 to 7.6 does not anticipate Applicants' inventive composition having a pH of from 8 to 9.

Clearly, Darko '530 fails to teach or suggest all the limitations of independent claim 1 and thus fails to anticipate the same.

Because the invention, as set forth in Applicants' claims, is not disclosed by the cited prior art, reconsideration and withdrawal of this rejection are respectfully requested.

Issues Under 35 U.S.C. § 103(a)

Claims 2-3 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Darko '530 in view of Gentile (U.S. 5,895,789) (hereinafter Gentile '789). This rejection is respectfully traversed.

The Examiner asserts that Gentile '789 teaches that alkylammonium salts of 2-arylpropionic acids, such as ketoprofen lysinate, are prepared for injection without preservatives, and maintains that one skilled in the art would be motivated to modify Darko '530 in view of Gentile '789.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally,

the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As discussed above, Darko '530 fails to teach or suggest all the limitations of the instant invention. In particular, Darko '530 fails to disclose a parenteral composition comprising an alkylammonium salt of a 2-arylpropionic acid in an aqueous solution at a pH of from 8 to 9. Gentile '789 fails to cure these deficiencies.

Gentile '789 discloses a pharmaceutical composition which contains alkylammonium salts of 2-arylpropionic acids. At page 3, lines 58-67, Gentile '789 discloses that "pH adjustment of the injectable solution between 7.0 and 7.5 brings about, not only a useful increment of osmolarity...but also an ulterior improvement in the stability of the darkening solution and in the turbidity...". Clearly, Gentile '789 explicitly teaches maintaining a pH of from 7.0 to 7.5. One skilled in the art, when faced with the teachings of Darko '530 and Gentile '789 would not be motivated to modify either one by adjusting the pH to a range of from 8 to 9, because none of the references provide a motivation to do so, and, furthermore, because there is no expectation of success.

Because neither Darko '530 nor Gentile '789, alone or in combination, teach or suggest all the limitations of the claimed invention, this rejection should be withdrawn.

Furthermore, assuming *arguendo* that Gentile '789 cured the deficiencies of Darko '530 (a point which Applicants do not concede), it is noted that references cannot be arbitrarily combined. There must be some reason why one of ordinary skill in the art would be motivated

to make the proposed combination of the primary and secondary references. *In re Nomiya*, 184 USPQ 607 (CCPA 1975). According to MPEP 2141(II)(B), the references must be considered as a whole and **must suggest the desirability and thus the obviousness of making the combination** (emphasis added). The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention (see MPEP 2141(II)(C)). Furthermore, the mere fact that references can be combined or modified does not render the resultant combination obvious. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) (emphasis in original).

The Examiner's attention is directed to columns 1 and 2 of Darko '530. Darko '530, while discussing prior art compositions, explicitly discusses the teachings of Gentile '789. Darko '530 asserts that Gentile '789 is not related to lysine salts of ibuprofen, to which Darko '530 is directed. Furthermore, Darko '530 asserts that there are several disadvantages to the composition of Gentile '789, including the need to buffer the composition with a C_3 to C_5 di- or tricarboxylic acid or an alkali or alkaline earth metal thereof. Furthermore, according to Darko '530, the composition of Gentile '789 must be packaged in dark glass containers opaque to light radiation.

Clearly, the primary reference of Darko '530 is teaching away from the combination made by the Examiner. In fact, the primary reference is teaching away from the exact combination of references made by the Examiner, even referring to the secondary reference by its U.S. Patent number. No stronger case can be made for the proposition that one of ordinary skill in the art, having fully read and understood the Darko reference, would not have been motivated to combine this reference with Gentile '789.

Because the instant invention, as set forth in Applicants' claims, is not disclosed or made obvious by the cited prior art, reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By _____

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